BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1A through 1E depict the schematic structure of the PAR1 receptor; membrane-tethered PAR1 i3-loop peptides of the present invention and their effect on the activation and/or regulation of Ca2+ signaling and aggregation in platelets. In FIG. 1A, the topological arrangement of the membrane-spanning segments (TM1-7), extracellular loops (e1-e4), and intracellular loops (i1-i4) of PAR1 is based on the X-ray structure of rhodopsin (*K. Palczewski et al., Science 289, 739-45 (2000)*) and is illustrated on the left. Thrombin cleaves the extracellular domain (e1) at the R41-S42 bond creating a new N-terminus, S42FLLRN, which functions as a tethered PAR1 agonist.

FIGS. 2A through 2G depict schematic representations of the alignment of i3 loops and adjacent transmembrane regions, as well as cell-penetrating ability of the peptides of the present invention.

FIGS. 3A through 3C depict the pepducin P1pal-19's inability to activate a C-tail deleted PAR1 and its ability to activate a PAR1 i3-mutant.

FIGS. 4A through 4E show that the pepducins of the present invention are full antagonists of their cognate receptors.

FIG. 5 shows that the peptides of the present invention penetrate intact cells.

FIGS. 6A through 6D shows the full specificity profiles of the PAR1 pepducins tested with six other GPCRs.

FIG. 7 depicts pepducin activation of the G_S-coupled MC4 obesity receptor.

FIG. 8 depicts LBS1 schema.

9/29/04 SLW FIG. 9A through 9E ~~FIG. 9~~ shows that LBS1-pepducin inhibits activation of PAR1.